

corollary belief that there are no differences in equilibrium solubility among the salts of a given drug in a specific cyclodextrin. This is explained in Applicant's specification on page 2, lines 14-27. As a consequence of the foregoing beliefs, the art nowhere discloses locating a salt having a solubility greater than a threshold solubility (i.e. greater than a desired target solubility), by Applicant's method or anything approaching it.

Claims 1 and 2 stand rejected under 35 USC 112, second paragraph, as being indefinite, for reasons of record. The Examiner stated, in pertinent part, in paragraph 6, page 2:

"Applicant argues against this rejection on the grounds that the term "desired target solubility" was completely clear and distinct without the abundant explanation given in Applicant's specification, but that, especially in light of the explanation (and exemplification) of "desired solubility" supplied by Applicant in the specification, one skilled in the art, would find the claims to be clear and distinct, and have no difficulty understanding the metes and bounds of the subject matter claimed. However, this argument is not persuasive since the metes and bounds of the term "desired target solubility" cannot be determined without further explanation in the claims as to the exact solubility that is desired by the Applicant. Furthermore, this terminology does not fulfill the requirement of 35 U.S.C. 112, second paragraph, since this language does not point out and distinctly claim the subject matter and the specification does not provide a standard for ascertaining the requisite degree of the term. [Page 2, paragraph 6 of the Official Action].

The rejection is traversed on the basis that one skilled in the art, particularly in view of the explanation and definition given in the specification, would readily understand the metes and bounds of the term "desired target solubility". It is noted that this is all that the second paragraph of § 112 requires - - that the claims set out and circumscribe a particular area that the applicant regards as the invention with a reasonable degree of precision and particularity.

The Examiner, as quoted above, has taken the position that Applicant's term "desired target solubility" does not point out and distinctly claim the invention because (1) the term cannot be determined without further explanation in the claims as to the exact solubility that is desired by the Applicant. and (2) the specification does not provide a standard for ascertaining the requisite degree of the term.

Applicant takes the position that (1) an Applicant is allowed to be his own lexicographer; (2) definiteness of claim language must be analyzed not in a vacuum, but in light of the specification and the prior art; *In re Marosi*, 218 USPQ 289 (Fed Cir 1983); and (3) Applicant has gone out of her way in her specification to explain and exemplify exactly what is intended. Further, explanation is not required to be placed

in the claims, as implicitly contended by the Examiner. Enablement and description, including explanation, are the functions of the specification. It is so well accepted as not to require citation that terms in the claims are interpreted in light of the specification. It is difficult to envision how one skilled in the art could miss the meaning intended by Applicant in the instant application in view of the extensive explanation given in the specification. Indeed, the application was originally drafted with an eye toward ensuring that the term "desired target solubility" would be well understood.

At page 4 line 25 to page 5, line 14, Applicant states

A "desired target solubility" as used herein can be a minimum solubility, usually pre-determined or pre-chosen, required for the compound being tested. The required minimum solubility will generally be chosen on the basis of therapeutic need. For example, assume that it is desired to administer 20 mg of a compound ("Compound X") parenterally, by injection, and that it is desired to administer an injection volume of not more than 2 ml to minimize pain on injection. Thus a salt of Compound X, in order to be "useful", would need to have a solubility, in the chosen aqueous cyclodextrin, equivalent to or greater than 10 mg/ml of Compound X in its active form.

Within a given series of salts, the most soluble salt may not be the most useful candidate for a given application. Factors such as chemical stability, hygroscopicity, and the potential for precipitation may also be considered and weigh in favor of choosing a candidate having a solubility greater than the target solubility, but less than the maximum determined within the series.

On the other hand, at times it may indeed be desired simply to find the salt with the highest solubility of all salts within a series of salts of a particular compound. In this case the "desired target solubility" is simply the highest solubility encountered in the series of salts by comparison of equilibrium solubilities among the various salt candidates. For example, if it is desired to make a dry oral dosage form such as a capsule or tablet using an inclusion complex of a salt of Compound X, then it may be desired simply to find the most soluble salt available in order to minimize the amount of inclusion complex in the dosage form, and thereby minimize the size of the dosage form itself.

The above text illustrates that Applicant has gone to great lengths to make sure that the phrase "desired target solubility" is fully understood within the context of the instant invention. The first paragraph notes that a desired target solubility will generally be some pre-determined or pre-chosen solubility selected on the basis of therapeutic need, and gives a hypothetical numerical example to illustrate exactly what is intended. The next paragraph explains that the salt having the maximum solubility determined within a series of salts may not always be selected simply because it is the maximum. Other factors, for example chemical stability, hygroscopicity, and the potential for precipitation, are mentioned which may weigh in favor of choosing a candidate having a solubility greater than the target solubility, but

less than the maximum solubility determined within a series of salts. The skilled art worker reading Applicant's disclosure would immediately realize that a "desired target solubility" is a solubility needed to effect therapeutic efficacy in a dosage form. The skilled worker would also realize that the actual salt selected need not be the most soluble salt found so long as its solubility meets or exceeds the target solubility.

Applicant further included a detailed example in the form of Example 3 which goes into great detail as to how salts having a desired target solubility would be chosen for adult and pediatric patient subsets when, because of differing therapeutic requirements for each different subset, the desired target solubility differs as well with respect to each subset. The example discloses a series of salts and explains exactly how desired target solubilities, and salts satisfying such targets, would be chosen. In view of Applicant's extensive description in the text and the examples offered to illustrate exactly what is intended, particularly Example 3, the Examiner is earnestly requested to reconsider the rejection. It is respectfully submitted that the rejection is simply not tenable for this application which, as noted above, was originally drafted to ensure that the term would in fact be well understood.

In view of the above comments, it is requested that the rejection under 35 USC §112 be withdrawn.

Claims 1-3 continue to be rejected under 35 USC 103(a) as being unpatentable over Bryant, US 5,624,940, Applicant's arguments from her previous response having been deemed not persuasive. The Examiner stated, in pertinent part:

...Applicants argument on pages 3 and 4 of their response filed November 29, 1999 is not persuasive since the metes and bounds of Applicants desired target solubility cannot be determined. The claims do not specific any particular salt of a compound and only indicated that the salts of the compound are being made soluble by combining the salts of the compound with cyclodextrin, which is well known in the art as indicated in the Bryant et al patent. The fact that Applicants are determining the solubility of a series of salts (which have not been specifically set forth in the claims) does not make the claims patentable over the prior art. Accordingly, the rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over the Bryant et al patent is maintained.

The rejection is traversed on the basis that Bryant does not disclose that different salts of the same compound have different solubilities in the same cyclodextrin, and, for that matter, teaches nothing relating to dermining any solubility above any minimum or threshold level.

So far as the Examiner's comments in paragraph 8 which relate to "the metes and bounds of Applicant's desired target solubility cannot be determined" are

concerned, Applicant's comments above relating to this issue are incorporated by reference. Applicant's method is intended to be general so that it can be used to find a useful salt (i.e., one having a solubility equal to or greater than a desired target solubility) for any compound. The method is not limited to any particular salts or to any particular compounds. Because of the method's generality, it would totally defeat the purpose of the invention to specify particular salts in the claims, and thereby limit the claims. It would be equally self-defeating to specify a particular "series of salts" in the claims. That would again needlessly limit the claims to that particular series of salts even though the invention does not reside in any particular series of salts. The point is that it would not be obvious to test a series of salts to see which one exceeds a pre-determined or desired (i.e., target) solubility if the art taught the salts would all have the same solubility in the first place.

Bryant does nothing to bridge the gap between the prior art and Applicant's invention. Bryant simply teaches a series of compounds, notes that the compounds can form the usual pharmaceutically acceptable acid addition and base addition salts, and discloses that cyclodextrin inclusion complexes can be made. Bryant discloses nothing about any one salt of a compound having a greater solubility in cyclodextrin than any other. Bryant discloses nothing about any method for making such a solubility determination within a series of salts, and fails to even remotely mention the feasibility for doing so. **There is emphatically no disclosure, teaching or recognition in Bryant that any salt of a given compound would be any more or less soluble in a given cyclodextrin than any other salt in the same cyclodextrin.** There is not even the slightest indication that different salts of the same compound can have different solubilities in a given cyclodextrin, i.e., of the very finding that underlies Applicant's invention.

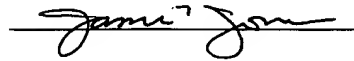
In summary, Bryant (1) never suggests that any particular salt of a compound of his formula (I) is any more soluble in a given cyclodextrin than any other salt made with any other acid or base also disclosed therein, (2) never touches on how such a salt would be located, and (3) never even remotely suggests the possibility or feasibility of doing so. Bryant neither discloses, suggests, nor motivates anything relating to Applicant's method, and could not without a recognition of Applicant's finding discussed above. Without such suggestion or motivation it is simply not possible for Bryant to render Applicant's method obvious. Accordingly, it is respectfully requested that the rejection of claims 1-3 over Bryant be withdrawn.

In view of the foregoing comments and amendments the Examiner is respectfully urged to reconsider and withdraw all rejections. It is believed this

application is in condition for allowance. A Notice of Allowance is accordingly
courteously solicited.

Respectfully submitted,

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James T. Jones
Attorney for Applicant
Reg. No. 30,561

Pfizer Inc
Patent Department
Eastern Point Road
Groton, CT 06340
(860) 441-4903